

REMARKS

At the onset, Applicants gratefully acknowledge the Examiner's courteous and professional efforts in the interview conducted with Applicants' representatives on July 30, 2002.

I. STATUS OF CLAIMS

Upon entry of this amendment, claims 47, 61-75, 78-79, and 81-83 are pending. Support for the amendment is found in the specification as filed, and in the international and French applications. For example, support for the amendment is found in original claim 14, and in the specification at page 11, lines 20-28. Accordingly, no new matter has been added.

II. The Claims Are Not Obvious Under 35 U.S.C. § 103

Yu in view of Coyle and Greenberger

The Office has rejected claims 47, 61-65, 67, 69-75, 78-79, and 81 under 35 USC§ 103(a) as being obvious over *Yu et al.* (U.S. Patent No. 5,506,133) ("*Yu*") in view of *Coyle et al.* (Science, 262:689-695, 1993) ("*Coyle*") and *Greenberger* (U.S. Patent No. 5,599,712) ("*Greenberger*") for the reasons set forth on pages 3-6 of the Office Action. Applicants respectfully traverse the rejection.

To establish a *prima facie* case of obviousness, the Examiner must demonstrate that there is some suggestion or motivation, either in the cited references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify a reference or combine reference teachings. M.P.E.P. § 2143.

In the present case, Applicants contend that the Examiner has failed to make a *prima facie* case of obviousness because this requirement has not been met.

As a basis for its rejection, the Office alleges that *Yu* "recites that defective human CuZn SOD-1 has been linked to familial ALS and that expression of a SOD gene (SOD-4) which is structurally and functionally related to SOD-1 can be used to treat human diseases involving excess free radicals." (Office Action, page 3.) The Office admits that *Yu* "does not teach the specifics of generating adenoviral vectors capable of expressing SOD-1 genes and does not provide a review of the roles of different SODs in reducing the levels of free radicals in humans." (*Id.*) The Office alleges that the secondary references, *Coyle* and *Greenberger*, "simply provide teachings on the specifics of generating adenoviral vectors (these procedures are well known in the art) and provide a review of the link between free radicals and disease in humans." (*Id.*, pages 4-5.) The Office concludes that it would have been obvious to combine *Yu*, *Coyle*, and *Greenberger*.

because *Yu et al.* specifically teaches that adenoviral vectors (which can be made by the methods disclosed by *Greenberger et al.*) can be used to deliver an SOD gene functionally and structurally related to SOD-1 to target cells for the express purpose of alleviating diseases marked by defective levels of SODs and an excess of free radicals and because *Coyle et al.* indicates that an increase in SOD-1 expression reduction can reduce the levels of free radicals and possibly alleviate some human diseases characterized by excess free radical levels.

(*Id.*, page 6.)

The Federal Circuit requires a showing of a suggestion or motivation to modify the teachings of prior art references. See, e.g., *In re Dembiczak*, 50 USPQ.2d 1614 (Fed. Cir. 1999). Modifying prior art references without evidence of such a suggestion or motivation simply takes the inventor's specification as a blueprint for

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piecing together the prior art to defeat patentability, which is the essence of hindsight. *Dembiczak*, 50 USPQ.2d at 1617. This is why the Federal Circuit places a burden on the Office to present "clear and particular" evidence showing motivation to combine or modify. *Id.* at 1617.

In this application, *Yu* does not teach or suggest administering a replication defective, recombinant adenovirus comprising a DNA sequence which encodes superoxide dismutase-1 (SOD-1) for treating the diseases recited in claim 47 as amended. Even if the SOD-1 gene and SOD-4 gene are functionally and structurally related as alleged by the Office, Applicants contend that one of ordinary skill in the art reading *Yu*, *Coyle*, and *Greenberger* would not have been motivated to substitute *Yu*'s SOD-4 sequence with Applicant's SOD-1 sequence to devise the presently claimed method of treating the specific recited diseases, particularly in light of the Office's admission that *Yu* "does not teach the specifics of generating adenoviral vectors capable of expressing SOD genes and does not provide a review of the roles of different SODs in reducing the levels of free radicals in humans." (Office Action, page 3.)

Applicants submit that the Office has not presented "clear and particular" evidence showing that one of ordinary skill in the art would have been motivated to modify the teaching of *Yu* to arrive at the claimed invention. Accordingly, Applicants respectfully request that the Office reconsider and withdraw the rejection.

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Yu in view of Coyle, Greenberger, and Engelhardt

The Office has rejected claims 66 and 82 under 35 USC§ 103(a) as being obvious over *Yu* in view of *Coyle, Greenberger, and Engelhardt et al.* (PNAS, 91:6196-6200, 1994) ("*Engelhardt*") for the reasons set forth on pages 6-7 of the Office Action. Applicants respectfully traverse the rejection.

Applicants incorporate by reference the above argument directed to *Yu, Coyle, and Greenberger*, and submit that *Engelhardt* does not provide any "clear and particular" evidence showing that one of ordinary skill in the art would have been motivated to modify the teaching of *Yu* to arrive at the claimed invention.

Accordingly, Applicants respectfully request that the Office reconsider and withdraw the rejection.

In addition, new claim 83 recites an adenovirus comprising ITR sequences and an encapsidation sequence, and wherein the E1 gene and at least one of the E4 or L1-L5 genes is non-functional. In order to support a *prima facie* case of obviousness, the cited references must teach or suggest all of the claim limitations. The Office has not presented any evidence that the references teach or suggest an adenovirus comprising ITR sequences and an encapsidation sequence, and wherein the E1 gene and at least one of the E4 or L1-L5 genes is non-functional. Accordingly, claim 83 is not *prima facie* obvious in view of the cited references.

Yu in view of Coyle, Greenberger, and Le Gal La Salle

The Office has rejected claim 68 under 35 USC§ 103(a) as being obvious over *Yu* in view of *Coyle, Greenberger, and Le Gal La Salle et al.* (Science, 259:988-990,

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1993) ("*Le Gal La Salle*") for the reasons set forth on pages 8-9 of the Office Action.

Applicants respectfully traverse the rejection.

Applicants incorporate by reference the above argument directed to *Yu*, *Coyle*, and *Greenberger*, and submit that *Le Gal La Salle* does not provide any "clear and particular" evidence showing that one of ordinary skill in the art would have been motivated to modify the teaching of *Yu* to arrive at the claimed invention.

Accordingly, Applicants respectfully request that the Office reconsider and withdraw the rejection.

III. CONCLUSION

In view of the foregoing, Applicants respectfully request that the Office reconsider and withdraw the rejections of pending claims 47, 61-75, 78-79, and 81-82 as obvious over the cited art, and allow all pending claims.

Please grant any extensions of time required to enter this amendment and response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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